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| 09/889,802 | 09/17/2001 | Roland Kreutzer | 33796 | 8835 |

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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER

WHITEMAN, BRIAN A

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| ART UNIT | PAPER NUMBER |
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1635

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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|------------------------------|--------------------------------------|--|--|
| Office Action Summary | Application No. 09/889,802 | Applicant(s) KREUTZER ET AL. | |
| | Examiner Brian Whiteman | Art Unit 1635 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 221-225, 232-239, 241-245 and 247-251 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 221-225, 232-239, 243, 245 and 248-251 is/are rejected.
- 7) ☒ Claim(s) 241, 242, 244 and 247 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Final Rejection

Claims 221-225, 232-239, 241-245, 247-251 are pending examination.

Applicants' traversal, the amendment to claims 221-224, 232, 236-238, 242, 243, 245, 247, and the addition of claims 248-251 in paper no. filed on 9/23/03 is acknowledged and considered.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in German on 1/30/99 and 11/24/99. It is noted that applicant has filed a certified copy of the 19903713.2 and 19956568.6 applications as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The patent (DE 196 18 797 C2) filed in the information disclosure statement filed 10/27/03 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Response to Arguments

Applicant's arguments, see, filed 9/23/03, with respect to 112 first paragraph rejection have been fully considered and are persuasive. The rejection of claims 232-238, 245 and 247 has been withdrawn because of the amendment to the independent claims to recite "An isolated mammalian cell."

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 249 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 249 recites the limitation "said double stranded region". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

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has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 221, 223, and 224 remain and claim 249 is rejected under 35 U.S.C. 102(b) as being anticipated by Alfonzo et al. (Nucleic Acid Research, Vol. 25, 3751-3759, 1997). Alfonzo teaches a double stranded RNA (dsRNA), wherein one strand has a region which is complementary to an RNA transcript of at least part of a mammalian gene, and the dsRNA comprises a 3' overhang, wherein the RNA strands are linked together (page 3755).

Applicant's arguments filed 9/23/03 have been fully considered but they are not persuasive for the reason set forth above.

With respect to applicant's argument that, "the overall length of the duplex structure is not taught nor is the length of the region of the complementarity (page 9)," the argument is not found persuasive because the term "comprising" and "having" means that any dsRNA that comprises a region that is complementary to an RNA transcript of a mammalian gene and the region is not more than 49 nucleotides anticipates the claimed product. Alfonzo teaches a dsRNA with a 3'-oligo(u) tail that is complementary or has a region (3'-oligo(u) tail) that is fully complementary to a mammalian RNA transcript.

Applicant's arguments that, "Alfonzo does not teach an actual oligoribonucleotide itself, but only teaches schematic models of duplexes which are incorporated into at least two models of RNA editing" and "the oligoribonucleotide taught by Alfonzo does not comprise a double stranded structure which is complementary to an RNA transcript of a mammalian target gene," appear to contradict each other because the applicant is stating the Alfonzo does and does not teach an oligoribonucleotide. Clarification is requested.

Furthermore, with respect to applicant's argument that, "Alfonzo does not teach an actual oligoribonucleotide itself, but only teaches schematic models of duplexes which are incorporated into at least two models of RNA editing", the argument is not found persuasive because MPEP 2121.04 recites, "Pictures and drawings may be sufficiently enabling to put the public in the possession of the article pictured." In view of MPEP 2121.04 and 2122, the argument is not found persuasive.

In response to applicant's argument that, "the dsRNA taught by Alfonzo cannot specifically inhibit the expression of a mammalian target gene (page 9)" and "Because a region of complementarity of only a few bases in a trypanosome mRNA would not be sufficient to specifically inhibit the expression of the mammalian target gene (page 10)," the argument is not found persuasive because MPEP § 716.01(c) states:

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the

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date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

In addition, MPEP 2112.01 recites, "If the composition is physically the same, it must have the same properties."

With respect to the argument that, "Alfonzo does not anticipate independent claims 232 and 237 (page 10)," is moot because claims 232 and 237 were not rejected as anticipated by Alfonzo.

Claims 221, 222, 223, 224, 225, 232, 233, 234, 235, 236, 237, 238, 239, 243, and 245 remain and claims 248, 249, 250, and 251 are rejected under 35 U.S.C. 102(e) as being anticipated by Kmiec et al. (US Patent 6,573,046, EFD 5/12/98). Kmiec teaches a recombinagenic oligonucleobase characterized by being a duplex nucleotide, including nucleotide derivatives or non-nucleotide interstrand linkers, and having between 20 and 120 nucleobases or equivalently between 10 and 60 Watson-Crick nucleobase pairs (column 4). In a preferred embodiment, the recombinagenic oligonucleobase is substantially a duplex and contains a single 3' end and 5' end; accordingly, the strands of the duplex are covalently linked by oligonucleobase or non-oligonucleobase linkers (column 4 and column 11). A further embodiment of the present invention is based on the discovery that the Non-Chimeric Mutational Vector (NCMV), according to Kumar, are effective substrates for the strand transfer and repair enzymes of eukaryotic and, specifically mammalian cells (column 4 and column 15). Kmiec further teaches that nucleobases are ribo-type (column 7 and column 8, lines 47-61). Furthermore, Kmiec teaches that the first and second strands consist of at least two regions that

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are homologous to a target gene, preferably between 30 and 45 (column 8, lines 26-46). In addition, Kmiec teaches that the oligonucleobase can have a 3' overhang (column 10, lines 40-67). The oligonucleobase can comprise a nuclease resistant nucleobase or 3' exonuclease protection or a polyethylene glycol linker (column 9, line 29-column 10, line 39).

Applicant's arguments filed 9/23/03 have been fully considered but they are not persuasive for the reason set forth above.

With respect to applicants' arguments that, "Kmiec discloses that the nucleic acid must be one continuous strand forming a hairpin and can not be two separate strands (pages 10 and 11)," is not found persuasive because Kmiec teaches that one or both strands can contain ribo-type nucleobases (column 8, lines 47-48). Furthermore, Kmiec teaches that the first and second strands can be linked covalently (column 9, lines 22-24). Kmiec teaches that a strand divided into two chains that are linked covalently through the alternative strand but not directly to each other (column 10, lines 42-67). This indicates that Kmiec teaches two separate RNA strands.

With respect to applicants' arguments that, "Kmiec cannot be full complementary to the transcript of the target gene (pages 11-12)," is not found persuasive because Kmiec teaches the sequence of the first and second strands consists of at least two regions that are homologous to the target gene (column 8, lines 29-32).

With respect to applicants' argument that, "the DMA exemplified by Kmiec confers a nucleotide mutation in the non-mammalian kanamycin resistance gene in bacteria" and "Since the DMV is complementary in part to a non-mammalian target DNA, the DMA is structurally distinct from the claimed oligoribonucleotide, which is fully complementary to an RNA transcript of a mammalian gene (page 12)," is not found persuasive because the term

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“comprising” and “having” means that any dsRNA that comprises a region that is complementary to an RNA transcript of a mammalian gene and the region is not more than 49 nucleotides anticipates the claimed product. Furthermore, Kmiec teaches that the sequence of the first and second strands consists of at least two regions that are homologous to the target gene (column 8, lines 29-32). Kmiec teaches targeting the oligoribonucleotide to a target sequence in a eukaryotic cell (columns 16-18).

With respect to applicants’ arguments that, “Kmiec et al does not demonstrate that said DMV with its interrupted regions of complementarity, specifically inhibits the expression of the mammalian target gene (page 12),” is not found persuasive because MPEP § 716.01(c) states:

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

In addition, MPEP 2112.01 recites, “If the composition is physically the same, it must have the same properties.”

Conclusion

Claims 241, 242, 244 and 247 are free of the prior art of record.

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Claims 241, 242, 244 and 247 remain objected to as being dependent upon a rejected base claim (claim 221), but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE - Art Unit 1635, can be reached at (703) 306-3217.

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Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635


KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER